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Abstract: Glucose, the body's primary source of energy, is sugar that is derived from carbohydrate foods. Glucagon, a peptide hormone generated in the pancreas, plays a key role in maintaining regular levels of glucose in the blood. Similar to insulin, glucagon is produced by cells in the pancreas. However, insulin and glucagon have opposite effects. When people eat, their blood sugar level increases. To reduce the blood sugar level, the pancreas releases insulin, which removes the sugar from the food and transports it to the respective cells so it can be transformed into energy. This process brings the blood sugar level back down. Conversely, glucagon's main purpose is to increase blood glucose levels. When blood glucose level begins to dip below the normal amount, more glucose needs to be found and pumped into the blood. Glucagon makes this possible by signaling the liver, which dispenses glucose. From a medicinal viewpoint, glucagon is manufactured as a life-saving drug, chiefly used to treat acute hypoglycemia, or very low blood sugar.

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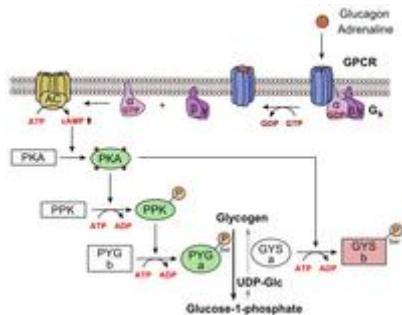
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Glucagon

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Glucose, the body's primary source of energy, is sugar that is derived from carbohydrate foods. Glucagon, a peptide hormone generated in the pancreas, plays a key role in maintaining regular levels of glucose in the blood. Similar to insulin, glucagon is produced by cells in the pancreas. However, insulin and glucagon have opposite effects. When people eat, their blood sugar level increases. To reduce the blood sugar level, the pancreas releases insulin, which removes the sugar from the food and transports it to the respective cells so it can be transformed into energy. This process brings the blood sugar level back down. Conversely, glucagon's main purpose is to increase blood glucose levels. When blood glucose level begins to dip below the normal amount, more glucose needs to be found and pumped into the blood. Glucagon makes this possible by signaling the liver, which dispenses glucose. From a medicinal viewpoint, glucagon is manufactured as a life-saving drug, chiefly used to treat acute hypoglycemia, or very low blood sugar.





Glucagon metabolic pathway to activate glycogen By FrozenMan (Own work) [CC BY-SA 4.0 (<http://creativecommons.org/licenses/by-sa/4.0>)], via Wikimedia Commons

Background

In 1922, while separating insulin from watery pancreas extracts, scientists John Murlin and Charles Kimball came upon a substance they regarded as having a distinct impact on low blood sugar. This substance was named *glucagon*. Many years after this discovery, researchers found it difficult to isolate and purify glucagon. Studies continued for nearly 30 years until researcher William Bromer and his associates finally sequenced and purified the substance.

Although the connection between insulin and glucagon has become an extensively studied area of endocrinology and biochemistry, early researchers were more interested in insulin due to its role in controlling diabetes. During early research of insulin, a swift transitory hyperglycemia was detected in animals that were injected with certain pancreatic extracts. The liver was shown as the site of the hyperglycemic activity. It was then discovered that insulin causes glycogenolysis—which happens when blood sugar level declines—in liver slices. Researchers then began to search for ways to facilitate intensive study concerning the mechanism of this effect. It took almost 30 years for Bromer and his associates to deliver a pure version of glucagon, and the substance has undergone considerable advancement since then. Besides being isolated in crystalline form, its structure has been fully determined, and its hypoglycemic effects are well defined.

Glucagon has distinct effects in the liver and other areas of the body. When blood sugar level starts to drop, glucagon is crucial to restoring it to its normal range. Glucagon controls two vital metabolic pathways in the liver that allow the liver to release glucose to the rest of the body. Under the first method of action, glucagon breaks down glycogen, a molecule in the body that stores glucose in the liver. Specifically, when blood sugar levels begin to drop, glucagon is released via the activation of enzymes that break down glycogen and produce glucose. The second method of action allows glucagon to activate gluconeogenesis, which is the pathway that enables non-hexose substrates, such as lipids and amino acids, to be changed into glucose; this method provides the bloodstream with an additional source of glucose.

Glucagon is also vital to the brain, which uses a significant amount of energy but contains only a limited amount of glycogen and relies on the bloodstream for a constant supply of glucose.

Overview

The glucagon hormone is made up of twenty-nine amino acids. Carbohydrate-rich foods—such as sweets, bread, potatoes, fruit, milk, and cereal—are the body's main source of glucose. When people eat these types of foods, the bloodstream absorbs glucose and moves it to the body's cells. If more glucose than the body needs at the time is consumed, the extra glucose is stored in the liver and muscles as glycogen. Notably, not eating enough carbohydrates will deplete glycogen. Between meals, glycogen can be used by the body for energy.

When the blood glucose level begins to decline, the glucagon receptor, which is located in the liver, signals the liver to break down and release glucose into the bloodstream.

As a medication, glucagon is a synthetic, manufactured version of the glucagon hormone. Although glucagon is primarily used to treat severe hypoglycemia, it is also used as a diagnostic tool in gastrointestinal radiology. In the latter case, glucagon is used to relax the gastrointestinal tract prior to radiologic examinations. Like insulin, glucagon is an important hormone that enables the body to maintain blood sugar, or glucose, in a narrow range. Whether an individual has hyperglycemia, diabetes, or another type of sugar-related ailment is ultimately determined by the insulin and glucagon production of his or her pancreas.

People with hyperglycemia may exhibit a range of symptoms, including blood glucose level above 180 mg/dL, frequent urination, blurry vision, difficulty concentrating, dizziness, sleepiness, anxiety, and confusion. In diabetic persons, hyperglycemia can occur as a side effect to certain diabetes medications, such as chlorpropamide, glimepiride, glipizide, glyburide, and nateglinide. Specific drugs, such as danazol, insulin, gastrin, and glucocorticoids, may increase glucose levels. Notably, levels can also increase after extended fasting or moderate to rigorous exercise. Drugs that may decrease glucose levels include secretin, propranolol, and atenolol.

Because glucagon is reported to be metabolized by the kidneys, renal failure is linked to elevated glucose level. When the body rejects a transplanted kidney, one of the first indicators may be high glucose levels. In patients with cardiac disease, glucagon may elevate blood pressure, pulse rate, and the demand for oxygen, all of which may be life threatening. In patients with pheochromocytoma, an adrenal gland tumor, glucagon can cause the tumor to produce catecholamines, resulting in a sudden and significant hike in blood pressure. Catecholamines are hormones generated by adrenal glands.

Glucagon is generally administered via injection under the skin, in the vein, or in the muscle. The drug comes in powder and liquid forms, which are combined prior to administration. Intravenous effects are reported to be virtually instantaneous, within 15 to 30 seconds. Intramuscular effects generally start within five to 15 minutes.

Prior to using glucagon, patients should tell their physicians whether they are allergic to any medications or foods, types of prescription and nonprescription substances they are taking, including vitamins, and whether they have a health condition (for example, being pregnant).

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